

**REMARKS**

Claims 1-2, 4-7, and 9-25 were pending prior to this Response. By the present communication, no new claims have been added, claim 11 has been canceled without prejudice or disclaimer, and claims 1, 4, 9-10, 13-21, and 23-24 have been amended to define the claims with greater particularity and/or correct typographical errors. Support for the amendments may be found throughout the specification as originally filed e.g., at least at paragraphs [0051], [0061], [0062], and [0064], as well as original claims 1 and 11-13 of the published specification (PCT Publication No. WO 2005/003137). No new matter has been added. Accordingly, upon entry of the present amendment, claims 1, 2, 4-7, 9-10, and 12-25 will be pending and under consideration in this application.

Applicants wish to thank Examiner Powers for her time and suggestions during the telephonic interview held on November 22, 2011 between Examiner Powers and Applicants' representative, during which the outstanding rejections were discussed. Applicants submit that the amendments and arguments presented herein address the substance of the interview.

**Rejection under 35 U.S.C. §112, 1<sup>st</sup> Paragraph**

Applicants respectfully traverse the rejection of claims 10-23 under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement. The Office Action states in pertinent part (on page 2) that "[t]here is no antecedent basis in the specification for a method for 'treating a refractile mammalian cancer *cell*' or the specific cancer *cells* set forth in claim 13." (emphasis added). The Office Action acknowledges, however, (on page 3) that the specification is enabling for salinosporamides as excellent candidates for use in the treatment of various human cancers, especially slow growing refractile cancers, stating "[t]hus, 'refractile cancers' are being treated with salinosporamides" as opposed to "refractile mammalian cancer *cells*." (emphasis added).

Without acquiescing to the reasoning provided by the Office Action, and in order to expedite prosecution, claim 10 has been amended to recite a method of treating a human refractile cell proliferative disorder, comprising contacting human refractile cancer cells with a therapeutically effective amount of a compound of the structure (I). Similarly, claims 13-20 have been amended to remove the term "refractile cancer cell," which has been replaced with the phrase "refractile cell proliferative disorder." Support for the amendments may be found throughout the originally filed specification e.g., at least at paragraph [0051] on page 17; paragraph [0062] on page 20; and Example 2 (disclosing bioactivity assays) on page 30 of the published application WO 2005/003137 and originally filed claims 10, 11, and 13. In particular, paragraph [0062] on page 20 describes the presently claimed method for "treating a mammalian cell proliferative disorder" and discloses each of the cell proliferative disorders recited in claim 13.

Furthermore, Applicants have previously submitted, with the response filed June 9, 2011, a declaration under 37 C.F.R. § 1.132 by Dr. Michael Palladino of Nereus Pharmaceuticals (licensee of the present application) providing patent and scientific literature confirming compounds of the structural formula (I) are useful in treating refractile cell proliferative disorders.

In view of the foregoing amendments and discussion, Applicants respectfully request reconsideration and withdrawal of the rejection.

**Rejection under 35 U.S.C. §112, 2<sup>nd</sup> Paragraph**

Applicants respectfully traverse the rejection of claims 9-23 under 35 U.S.C. 112, second paragraph, on the basis of alleged indefiniteness. In particular, the Office Action appears to take issue with the phrase "one additional anti-neoplastic agent" in dependent claim 9, stating (on page 3) that the phrase "renders the claim indefinite because neither claim 9 nor claim 7, on which it is dependent states that the pharmaceutical composition comprises a first anti-neoplastic agent." The rejection, and the reasoning forming the substantive basis therefore, is reiterated with regard to claim 23 and claim 10 on which it depends.

Applicants have amended claims 9 and 23, without acquiescence, to omit the term "additional" to address the indefiniteness rejection in the interest of advancing prosecution. Applicants have added the phrase "combination with at least one compound of claim 1." Support for the amendments may be found at least at paragraph [0064] on page 21 of the published application. Accordingly, Applicants respectfully request the rejection, as it applies to claims 9, 23, and claims dependent thereon, be withdrawn.

**Rejections under 35 U.S.C. § 102**

Applicants respectfully traverse the rejection of claims 1, 2, 4 to 7, 24 and 25 under 35 U.S.C. §102(a) and § 102(e) as allegedly being anticipated by Fenical et al. (WO 2002/047610 filed on November 16, 2001 and published on June 20, 2002; hereinafter "Fenical '2002").

In particular, the Office Action alleges (page 4) "[t]he reference discloses that Salinosporamide A was isolated and obtained in pure form [and this] compound corresponds to the claimed compound of the structure (I) wherein E<sub>1</sub>, E<sub>3</sub>, and E<sub>4</sub> are O; R<sub>1</sub> is chlorinated alkyl; R<sub>2</sub> is methyl; R<sub>3</sub> is hydroxyl; E<sub>2</sub> is -NH-; and x is 0. The reference also discloses Salinosporamide A in a pharmaceutical composition."

According to M.P.E.P. § 715.01(c), where the applicant is one of the co-authors of a publication cited against his or her application, he or she may overcome the rejection by filing a specific affidavit or declaration under 37 C.F.R. §1.132 establishing that the article is describing applicant's own work. An affidavit or declaration by applicant alone, indicating that applicant is the sole inventor and that the others were merely working under his or her direction, is sufficient to remove the publication as a reference under 35 U.S.C. 102(a). *In re Katz*, 687 F.2d 450, 215 USPQ 14 (CCPA 1982).

Applicants respectfully submit a declaration under 37 C.F.R. §1.132 by Dr. William Fenical, Dr. Paul R. Jensen, Dr. Robert H. R. Feling, and Dr. Tracy J. Mincer, establishing that Fenical '2002 describes the inventors' own work. Accordingly, Fenical '2002 is not available as prior art against the subject application, and withdrawal of the rejection is respectfully requested.

**Rejections under 35 U.S.C. § 103**

Applicants respectfully traverse the rejection of claims 9-25 under 35 U.S.C. §103(a) as allegedly being unpatentable over Fenical et al. (WO 2002/047610) in view of Wu et al. (WO 1999/022729; hereinafter “Wu”), Dick et al. (Journal of Biological Chemistry, 271(13), 7273-7276, 1996; hereinafter “Dick”), and Ogiso et al. (Cancer Research, 60, 2429-2434, 2000; hereinafter “Osigo”).

As discussed above, Applicants submit herewith a declaration under 37 C.F.R. §1.132 by Dr. William Fenical, Dr. Paul R. Jensen, Dr. Robert H. R. Feling, and Dr. Tracy J. Mincer, establishing that the Fenical ‘2002 reference describes the inventors’ own work. Accordingly, Fenical ‘2002 is no longer available as prior art under 35 U.S.C. §103. See M.P.E.P. §2141.01.

With regard to Wu, the Office Action relies on Wu as allegedly generally disclosing that proteasome inhibitors, such as lactocystin and analogues thereof can be used for treating cancer and can be used in combination with other pharmaceutical agents. The Office Action further relies on Dick stating that this document discloses that clasto-lactacystin  $\beta$ -lactone is the active intermediate lactacystin analog that interacts with the proteasome. Finally, the Osigo is offered by the Office Action as a reference that describes lactacystin as a new therapeutic agent to circumvent resistance to topo-II targeted chemotherapy in solid tumors. Based on the foregoing, the Office Action concludes “[i]t would have been obvious to one of ordinary skill in the art to use Salinosporamide A which is structurally similar to clasto-lactacystin  $\beta$ -lactone for the treatment of refractory or refractile cancer cells since lactacystin and analogs thereof are proteasome inhibitors that can be used to treat cancer.”

Applicants respectfully submit that neither Wu, Dick, nor Osigo, either alone or in combination, teach each and every element of the instant claims i.e., a pharmaceutical composition comprising a structural analog of Salinosporamide A (a compound of formula (I)) and at least one anti-neoplastic agent or a method of treating a human refractile cell proliferative disorder with a compound of formula (I). Since Fenical ‘2002 is not available as prior art and Wu, Dick, and Osigo fail to disclose or suggest all of the recited claim limitation *no prima facie*

case of obviousness is established. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

**Double-Patenting Rejection**

Applicants respectfully traverse the provisional rejection of claims 10-23 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-18 of copending Application No. 11/966,801.

As an initial matter, Applicants make note of the correction of the typographical error with regard to the co-pending application cited in the Office Action dated August 26, 2011. During Applicants' telephonic interview with the Examiner, Applicants were informed that claims 10-23 stand provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over Application No. 11/966,801, not 11/996,801.

Applicants respectfully submit that U.S. Patent Application No. 11/966,801 has been abandoned as evidenced by the Notice of Abandonment dated October 11, 2011. Accordingly, Applicants respectfully request the rejection be withdrawn.

Applicants respectfully traverse the provisional rejection of claims 1, 2, 4-7, 24 and 25 on the ground of nonstatutory obviousness-type double patenting as allegedly being unpatentable over claims 1-18 of copending Application No. 12/638,860 (hereinafter the '860 application).

While not acquiescing to the substantive basis for this rejection and in order to reduce the issues and expedite prosecution, a terminal disclaimer in compliance with 37 C.F.R. § 1.321(c), which disclaims the terminal part of the statutory term of any patent granted on the instant application which would extend beyond the expiration date of the full statutory term of the '860 application is submitted herewith. Applicants respectfully request that the Examiner reconsider the requirement for the terminal disclaimer upon allowance of the pending claims given that the '860 application is also a pending application with claims that are subject to amendment. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

Applicants respectfully traverse the rejection of claims 1, 2, 4-7, 9, 24 and 25 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 7,176,232 (hereinafter the '232 patent) and claims 1-4 of U.S. Patent No. 7,928,138 (hereinafter the '138 patent).

Applicants respectfully traverse the rejection of claims 10-23 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-3 of U.S. Patent No. 7,176,233 (hereinafter the '233 patent) and claims 1-27 of U.S. Patent No. 7,635,712 (hereinafter the '712 patent).

Applicants respectfully traverse the rejection of claim 9 on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15 of U.S. Patent No. 7,179,834 (hereinafter the '834 patent).

While not acquiescing to the substantive basis for this rejection and in order to reduce the issues and expedite prosecution, a terminal disclaimer in compliance with 37 C.F.R. §1.321(c), which disclaims the terminal part of the statutory term of any patent granted on the instant application that would extend beyond the expiration dates of the full statutory term of the 7,176,232; 7,928,138; 7,176,233; 7,635,712; and 7,179,834 patents are submitted herewith. Accordingly, reconsideration and withdrawal of this rejection are respectfully requested.

**CONCLUSION**

In view of the above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicants' undersigned representative if there are any questions relating to this application.

No fees are believed to be due with the filing of this response. However, the Commissioner is authorized to charge any fees deemed necessary with the filing of this paper, or credit any overpayments, to Deposit Account No. 07-1896 referencing the above-identified docket number.

Respectfully submitted,



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*Attachments:* Declaration under 37 C.F.R. § 1.132 by Dr. Robert H. R. Feling, Dr. William Fenical, Dr. Paul R. Jensen, and Dr. Tracy J. Mincer.